EXHIBIT F

US006951894B1

(12) **United States Patent**
Nicolson et al.

(10) **Patent No.: US 6,951,894 B1**
(45) **Date of Patent: *Oct. 4, 2005**

(54) **EXTENDED WEAR OPHTHALMIC LENS**

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(73) Assignee: **CIBA Vision Corporation**, Duluth, GA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

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Related U.S. Application Data

(63) Continuation of application No. 09/262,542, filed on Mar. 4, 1999, now abandoned, which is a continuation of application No. 09/108,714, filed on Jul. 1, 1998, now Pat. No. 5,965,631, which is a division of application No. 08/682,452, filed on Jul. 17, 1996, now Pat. No. 5,849,811, which is a division of application No. 08/569,816, filed on Dec. 8, 1995, now Pat. No. 5,760,100, which is a continuation-in-part of application No. 08/301,166, filed on Sep. 6, 1994, now abandoned.

(30) **Foreign Application Priority Data**

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(51) **Int. Cl.**[7] **C08K 3/00**
(52) **U.S. Cl.** **523/107**; 523/106; 523/108
(58) **Field of Search** 523/106, 107

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(57) **ABSTRACT**

An ophthalmic lens suited for extended-wear periods of at least one day on the eye without a clinically significant amount of corneal swelling and without substantial wearer discomfort. The lens has a balance of oxygen permeability and ion or water permeability, with the ion or water permeability being sufficient to provide good on-eye movement, such that a good tear exchange occurs between the lens and the eye. A preferred lens is a copolymerization product of a oxyperm macromer and an ionoperm monomer. The invention encompasses extended wear contact lenses, which include a core having oxygen transmission and ion transmission pathways extending from the inner surface to the outer surface.

84 Claims, No Drawings

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Bausch & Lomb Incorporated's Opposition to CIBA Corporation's Motion to Permit Certain Attorney's to have access to Information Under the Stipulated Protective Order (with Exhibits A–J) (Note: This Information is Subject to a Protective Order—It is not Open to the Public, but Only to the Examiner or Other Authorized Patent and Trademark Office Employee).

Defendant Bausch & Lomb Incorporated's Opposition to CIBA Corporation's Motion to Use Evidence from this case at the Reexamination Proceedings (with Exhibits A–J) (Note: This Information is Subject to a Protective Order—It is not Open to the Public, but Only to the Examiner or Other Authorized Patent and Trademark Office Employee).

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EXTENDED WEAR OPHTHALMIC LENS

This application is a continuation of Ser. No. 09/262,542, filed Mar. 4, 1999 now abandoned, which is a continuation of Ser. No. 09/108,714, filed Jul. 1, 1998, now U.S. Pat. No. 5,965,631 which is a divisional of application Ser. No. 08/682,452, filed Jul. 17, 1996, now U.S. Pat. No. 5,849,811 which is a divisional of application Ser. No. 08/569,816, filed Dec. 8, 1995 now U.S. Pat. No. 5,760,100 which is a continuation-in-part of U.S. application Ser. No. 08/301,166, filed on Sep. 6, 1994 now abandoned. Priority is also claimed 119 for German Application No. 95810221.2 filed on Apr. 4, 1995 and Swiss Application No. 1496/95 filed on May 19, 1995.

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates broadly to lenses and polymeric materials useful in optic and ophthalmic arts. More specifically, this invention relates to polymeric materials and treatment processes useful in the manufacture of contact lenses. Still more specifically, this invention relates to contact lenses useful as extended-wear contact lenses.

2. Description of the Related Art

A wide variety of research has been conducted in the field of biocompatible polymers. The definition of the term "biocompatible" depends on the particular application for which the polymer is designed. In the field of ophthalmic lenses, and in particular in the field of contact lenses, a biocompatible lens may be generally defined as one which will not substantially damage the surrounding ocular tissue and ocular fluid during the time period of contact. The phrase "ophthalmically compatible" more appropriately describes the biocompatibility requirements of ophthalmic lenses.

One ophthalmic compatibility requirement for contact lenses is that the lens must allow oxygen to reach the cornea in an amount which is sufficient for long-term corneal health. The contact lens must allow oxygen from the surrounding air to reach the cornea because the cornea does not receive oxygen from the blood supply like other tissue. If sufficient oxygen does not reach the cornea, corneal swelling occurs. Extended periods of oxygen deprivation causes the undesirable growth of blood vessels in the cornea. "Soft" contact lenses conform closely to the shape of the eye, so oxygen cannot easily circumvent the lens. Thus, soft contact lenses must allow oxygen to diffuse through the lens to reach the cornea.

Another ophthalmic compatibility requirement for soft contact lenses is that the lens must not strongly adhere to the eye. Clearly, the consumer must be able to easily remove the lens from the eye for disinfecting, cleaning, or disposal. However, the lens must also be able to move on the eye in order to encourage tear flow between the lens and the eye. Tear flow between the lens and eye allows for debris, such as foreign particulates or dead epithelial cells, to be swept from beneath the lens and, ultimately, out of the tear fluid. Thus, a contact lens must not adhere to the eye so strongly that adequate movement of the lens on the eye is inhibited.

While there exist rigid gas permeable ("RGP") contact lenses which have high oxygen permeability and which move on the eye, RGP lenses are typically quite uncomfortable for the consumer. Thus, soft contact lenses are preferred by many consumers because of comfort. Moreover, a contact lens which may be continuously worn for a period of a day or more (including wear during periods of sleeping) requires comfort levels which exclude RGP lenses as popular extended-wear candidates.

In order to balance the ophthalmic compatibility and consumer comfort requirements in designing a daily wear soft contact lens, polymers and copolymers of 2-hydroxyethyl methacrylate (HEMA) were developed. These hydrophilic polymers move well on the eye and provide sufficient oxygen permeability for daily wear. Certain soft contact lenses have been approved by the FDA for extended wear periods of up to about 6 nights of overnight wear and seven days of daily wear. However, the consumer cannot safely and comfortably wear these poly(HEMA) lenses for extended periods of seven days or more, because the oxygen permeability is insufficient. True extended wear (i.e., seven days or more) of these lenses may result, at a minimum, in corneal swelling and development of surface blood vessels in the cornea.

In order to improve oxygen permeability, polymers containing silicone groups were developed. A variety of siloxane-containing polymers have been disclosed as having high oxygen permeability. For example, see U.S. Pat. Nos. 3,228,741; 3,341,490; 3,996,187; and 3,996,189. However, polysiloxanes are typically highly lipophilic. The properties (e.g., lipophilicity, glass transition temperature, mechanical properties) of known polysiloxanes has resulted in contact lenses which adhere to the eye, inhibiting the necessary lens movement. In addition, polysiloxane lipophilicity promotes adhesion to the lens of lipids and proteins in the tear fluid, causing a haze which interferes with vision through the lens.

There have been attempts to blend the desirable hydrophilic properties of hydrophilic polymers, formed from monomers such as HEMA, with the desirable oxygen permeability of polymers formed from siloxane-containing monomers. For example, see U.S. Pat. Nos. 3,808,178; 4,136,250; and 5,070,169. However, prior attempts at producing a true extended wear contact lens have been unsuccessful, either because of the effect of the extended-wear lens on corneal health or because the lens would not move on the eye. Thus, there remains a need for an ophthalmically compatible, transparent polymeric material which is suited to extended periods of continuous contact with ocular tissue and tear fluid.

OBJECTS AND SUMMARY OF THE INVENTION

An object of the invention is to provide a material having a balance of oxygen permeability, ion permeability, on-eye movement and tear exchange, all of which are sufficient for corneal health and wearer comfort during extended periods of continuous wear.

Another object of the invention is to provide an ophthalmic lens capable of extended continuous wear periods of at least 24 hours without substantial adverse impact on ocular health or consumer comfort, and more preferably, to provide a lens capable of continuous wear of 4 to 30 days or more without substantial adverse impact on ocular health or consumer comfort.

A further object of the invention is to provide an ophthalmic lens capable of extended continuous wear periods of at least 24 hours without substantial corneal swelling or consumer discomfort, and more preferably, to provide a lens capable of continuous wear of 4, 7, 14 or 30 days or more without substantial corneal swelling or consumer discomfort.

Yet another object of the invention is to provide methods of forming an extended-wear ophthalmic lens.

Still a further object of the invention is to provide methods of testing and classifying ophthalmic lenses as candidates for true extended-wear.

These and other objects of the invention are met by the various embodiments described herein.

One embodiment of the invention is an ophthalmic lens, suited to extended periods of wear in continuous, intimate contact with ocular tissue and tear fluid. The lens displays a balance of oxygen permeability and ion permeability sufficient to maintain good corneal health, adequate movement of the lens on the eye and wearer comfort during extended wear periods. The lens is formed by polymerization, preferably copolymerization, of (a) at least one oxyperm polymerizable material which is capable of polymerizing to form a polymer having a high oxygen permeability; and (b) at least one ionoperm polymerizable material which is capable of polymerizing to form a polymer having a high ion permeability. Preferably, the lens includes a core polymeric material and ophthalmically compatible surfaces. In a preferred embodiment, the surface is more hydrophilic and lipophobic than the core polymeric material.

Another embodiment of the invention is a method of forming an ophthalmic lens having high oxygen permeability and high ion permeability. The method includes the step of forming a core material, having an inner surface and an outer surface, such that at least one pathway for ion transport and at least one pathway for oxygen transport are present from the inner to the outer surface. In a preferred embodiment, the method includes treating the surface of the lens to render the surface more hydrophilic than the core.

A further embodiment of the invention is an ophthalmic lens comprising a polymeric material which has a high oxygen permeability and a high ion or water permeability, the polymeric material being formed from at least one polymerizable material including (a) at least one oxyperm segment and (b) at least one ionoperm segment. The lens displays a balance of oxygen permeability and ion permeability sufficient to maintain good corneal health, adequate movement of the lens on the eye and wearer comfort during extended wear periods.

Yet another embodiment of the invention is a method of using a contact lens having both an oxygen transmission pathway and an ion transmission pathway from inner to outer surface as an extended wear lens. The method includes (a) applying the lens to the ocular environment and (b) allowing the lens to remain in intimate contact with the ocular environment for a period of at least 24 hours without substantial adverse impact on corneal health or wearer comfort. A preferred method includes additional steps of (c) removing the lens from the ocular environment; (d) disinfecting the lens; (e) applying the lens to the ocular environment; and (f) allowing the lens to remain in intimate contact with the ocular environment for a period of at least an additional 24 hours. In a preferred embodiment, the lens is worn for a continous period of at least seven days without substantial adverse impact on corneal health or wearer comfort.

OUTLINE OF DESCRIPTION OF THE PREFERRED EMBODIMENTS

DESCRIPTION OF THE PREFERRED EMBODIMENTS

One embodiment of the present invention is an ophthalmically compatible, transparent lens suited to extended periods of continuous contact with ocular tissue and tear fluids. A particularly preferred embodiment of the invention is an extended-wear vision correction lens suited for safe and comfortable long term wear without removal. In order to properly describe the invention and to delineate the metes and bounds of the claims, a set of basic terms will be defined at the outset.

I. DEFINITION OF TERMS

An "ophthalmic lens", as used herein, refers to lenses which are placed in intimate contact with the eye or tear fluid, such as contact lenses for vision correction (e.g., spherical, toric, bifocal), contact lenses for modification of eye color, ophthalmic drug delivery devices, ocular tissue protective devices (e.g., ophthalmic healing promoting lenses), and the like. A particularly preferred ophthalmic lens is an extended-wear contact lens, especially extended-wear contact lenses for vision correction.

A "polymerizable material which is capable of polymerizing to form a polymer having a high oxygen permeability", as used herein, refers to monomers, oligomers, macromers, and the like, and mixtures thereof, which are capable of polymerizing with like or unlike polymerizable materials to form a polymer which displays a relatively high rate of oxygen diffusion therethrough. For convenience of reference, these materials will be referred to herein as "oxyperm polymerizable materials" and the resultant polymers will be referred to herein as "oxyperm polymers".

The "oxygen transmissibility" of a lens, as used herein, is the rate at which oxygen will pass through a specific ophthalmic lens. Oxygen transmissibility, Dk/t, is conventionally expressed in units of barrers/mm, where t is the average thickness of the material [in units of mm] over the area being measured and "barrer" is defined as:

$$[(cm^3 \text{ oxygen})(mm)/(cm^2)(sec)(mm\ Hg)]\times 10^{-9}$$

The "oxygen permeability", Dk, of a lens material does not depend on lens thickness. Oxygen permeability is the rate at which oxygen will pass through a material. Oxygen permeability is conventionally expressed in units of barrers, where "barrer" is defined as:

$$[(cm^3 \text{ oxygen})(mm)/(cm^2)(sec)(mm\ Hg)]\times 10^{-10}$$

These are the units commonly used in the art. Thus, in order to be consistent with the use in the art, the unit "barrer" will have the meanings as defined above. For example, a lens having a Dk of 90 barrers ("oxygen permeability barrers") and a thickness of 90 microns (0.090 mm) would have a Dk/t of 100 barrers/mm ("oxygen transmissibility barrers"/mm).

A "polymerizable material which is capable of polymerizing to form a polymer having a high ion permeability", as used herein, refers to monomers, oligomers, macromers, and the like, and mixtures thereof, which are capable of polymerizing with like or unlike polymerizable materials to form a polymer which displays a relatively high rate of ion or water permeation therethrough. For convenience of reference, these materials will be referred to herein as "ionoperm polymerizable materials" and the resultant polymers will be referred to herein as "ionoperm polymers".

A "macromer", as used herein, refers to a polymerizable material which has a molecular weight of at least about 800 grams/mol. The term "macromer", as used herein, also encompasses oligomers.

A "monomer", as used herein refers to a polymerizable material which has a molecular weight of less than about 800 grams/mol.

A "phase", as used herein, refers to a region of substantially uniform composition which is a distinct and physically separate portion of a heterogeneous polymeric material. However, the term "phase" does not imply that the material described is a chemically pure substance, but merely that certain bulk properties differ significantly from the properties of another phase within the material. Thus, with respect to the polymeric components of a lens, an ionoperm phase refers to a region composed of essentially only ionoperm polymer (and water, when hydrated), while an oxyperm phase refers to a region composed of essentially only oxyperm polymer.

A "continuous phase" as used herein, refers to a region of substantially uniform composition which forms a continuous pathway from one surface of an article to another surface of an article.

"Co-continuous phases" , as used herein, refers to at least two regions, each of substantially uniform composition which differs from the other, and each of which forms a continuous pathway from one surface of an article to another surface of an article. Thus, an ophthalmic lens having co-continuous phases of oxyperm polymer and ionoperm polymer will have two continuous pathways or sets of continuous pathways extending from the inner surface of the lens to the outer surface of the lens.

"Morphology" , as used herein, refers to the structure and relationship of the phases of a material.

"Ophthalmically compatible" as used herein, refers to a material or surface of a material which may be in intimate contact with the ocular environment for an extended period of time without significantly damaging the ocular environment and without significant user discomfort. Thus, an ophthalmically compatible contact lens will not produce significant corneal swelling, will adequately move on the eye with blinking to promote adequate tear exchange, will not have substantial amounts of lipid adsorption, and will not cause substantial wearer discomfort during the prescribed period of wear.

"Ocular environment" as used herein, refers to ocular fluids (e.g., tear fluid) and ocular tissue (e.g., the cornea) which may come into intimate contact with a contact lens used for vision correction, drug delivery, wound healing, eye color modification, or other ophthalmic applications. "Hydrophilic" as used herein, describes a material or portion thereof which will more readily associate with water than with lipids.

A "hydrophilic surface " as used herein, refers to a surface which is more hydrophilic and lipophobic than the bulk or core material of an article. Thus, an ophthalmic lens having a hydrophilic surface describes a lens having a core material having a certain hydrophilicity surrounded, at least in part, by a surface which is more hydrophilic than the core.

The "outer surface" of a lens, as used herein, refers to the surface of the lens which faces away from the eye during wear. The outer surface, which is typically substantially convex, may also be referred to as the front curve of the lens. The "inner surface" of a lens, as used herein, refers to the surface of the lens which faces towards the eye during wear. The inner surface, which is typically substantially concave, may also be referred to as the base curve of the lens.

"TRIS" as used herein, refers to 3-methacryloxypropyltris (trimethylsiloxy) silane, which is represented by CAS No. 17096-07-0. The term "TRIS" also includes dimers of 3-methacryloxypropyltris(trimethylsiloxy) silane.

"Molecular weight" of a polymeric material (including monomeric or macromeric materials), as used herein, refers to the number-average molecular weight unless otherwise specifically noted or unless testing conditions indicate otherwise.

A. Oxyperm Polymerizable Materials

Oxyperm polymerizable materials include a wide range of materials which may be polymerized to form a polymer displaying a relatively high oxygen diffusion rate therethrough. In addition, these materials must be relatively ophthalmically compatible. These oxyperm polymerizable materials include, without limitation thereto, siloxane-containing macromers and monomers, fluorine-containing macromers and monomers, and carbon-carbon triple bond-containing macromers and monomers. The oxyperm macromer or monomer may also contain hydrophilic groups.

Preferred oxyperm polymers are those formed from a siloxane-containing macromer. Macromers having dialkyl siloxane groups, especially dimethyl siloxanes, are particularly preferred. These macromers are broadly referred to as poly(dimethyl siloxanes) (also, PDMS). The siloxane-containing macromer may also include hydrophilic groups. Examples of suitable siloxane-containing macromers include, without limitation thereto, the Materials A, B, C, and D as described herein.

The oxygen transmissibility (Dk/t) of the lens is preferably at least 70 barrers/mm, more preferably at least 75 barrers/mm, and most preferably at least 87 barrers/mm. The lens center thickness is typically more than about 30 microns, preferably about 30 to about 200 microns, more preferably about 40 to about 150 microns, even more preferably about 50 to about 120 microns, and most preferably about 60 to about 100 microns.

The oxygen transmissibility of the extended-wear lens from the outer surface to the inner surface must be sufficient to prevent any substantial corneal swelling during the period of extended wear. It is known that the cornea swells approximately 3% to 4% during overnight periods of sleep when the eyelids are closed, as a result of oxygen deprivation. It is also known that wearing a typical contact lens, such as ACUVUE (Johnson & Johnson), for a period of about 8 hours (overnight wear) causes corneal swelling of about 11%. However, a preferred extended-wear contact lens will produce, after wear of about 24 hours, including normal sleep periods, corneal swelling of less than about 8%, more preferably less than about 6%, and most preferably less than about 4%. A preferred extended-wear contact lens will produce, after wear of about 7 days, including normal sleep periods, corneal swelling of less than about 10%, more

preferably less than about 7%, and most preferably less than about 5%. Thus, the extended-wear lens must have oxyperm polymer in an amount sufficient to produce oxygen diffusion pathways from the outer surface to the inner surface of the lens which are sufficient to yield the above properties relating to corneal swelling. Preferably, the extended-wear lens has a continuous phase of oxyperm polymer extending from the outer surface to the inner surface of the lens.

B. Ionoperm Polymerizable Materials

Ionoperm polymerizable materials include a wide range of materials which may be polymerized to form a polymer displaying a relatively high ion diffusion rate therethrough. In addition, these materials must be relatively ophthalmically compatible. These ionoperm polymerizable materials include, without limitation thereto, acrylates and methacrylates, such as 2-hydroxyethyl methacrylate, acrylamide, methacrylamide, and dimethylacrylamide; poly (alkylene glycols), such as poly(ethylene glycol); N-vinyl pyrrolidones such as N-vinyl-2-pyrrolidone; and the like and mixtures thereof. Other ionoperm materials are disclosed in the specific embodiments of Materials A–D, described below.

C. Weight Ratios

The ratios of oxyperm to ionoperm polymerizable materials may vary substantially, depending on the selected balance of oxygen permeability and ion permeability for the chosen end-use of the molded polymeric article. Preferably, the volumetric ratio of oxyperm to ionoperm material (including water) in the fully hydrated lens is about 40 to about 60 to about 60 to about 40. However, weight percentages, based on the total weight of the lens, will be defined because weight percentages are more conveniently utilized in lens fabrication. Preferably, the extended-wear contact lenses having substantially only ionoperm and oxyperm materials will have about 60 to about 85 weight percent oxyperm polymerizable material and about 15 to about 40 weight percent ionoperm polymerizable material in the prepolymerization mixture, based on total polymerizable material weight. More preferably, the prepolymerization mixture will contain about 70 to about 82 weight percent oxyperm polymerizable material and about 18 to about 30 weight percent ionoperm polymerizable material, based on total polymerizable material weight.

A wide variety of additional polymerizable materials may be included in the mixture prior to polymerization. Cross-linking agents, such as ethylene glycol dimethacrylate (EGDMA), may be added to improve structural integrity and mechanical strength. Antimicrobial polymerizable materials such as poly(quaternary ammonium) salts may be added to inhibit microbial growth on the lens material. Also, additional ionoperm monomers or macromers and oxyperm polymerizable materials may be added to adjust the oxygen permeability and ion permeability of the final molded article. An especially advantageous polymerizable material is TRIS, which may act both to increase oxygen permeability and to improve the modulus of elasticity.

A preferred prepolymerization mixture will include (a) about 30 to 60 weight percent oxyperm macromer, (b) about 20 to 40 weight percent ionoperm polymerizable material, and (c) about 1 to 35 weight percent TRIS, based on the total lens weight. More preferably, the amount of TRIS is about 10 to 33 weight percent, based on the total prepolymerization mixture weight.

In a preferred embodiment, the prepolymerization mixture includes less than about 5 weight percent cross-linking agent, based on the total prepolymerization mixture weight. More preferably, the prepolymerization mixture includes less than about 2 weight percent cross-linking agent, based on the total prepolymerization mixture weight. Even more preferably, the prepolymerization mixture includes substantially no cross-linking agent. In a a particularly preferred embodiment, the prepolymerization mixture includes no added cross-linking agent.

The previously described ranges for oxyperm polymerizable materials, ionoperm polymerizable materials, and TRIS are offered to enable the reader to better comprehend the invention. However, it should be noted that the specific weight or volume percentages of oxyperm and ionoperm polymerizable materials are not the most critical factors to consider in preparing a good extended-wear ophthalmic lens. More importantly, the lens must have sufficient ion permeability for good on-eye movement and sufficient oxygen permeability for good corneal health during the extended wear period.

D. Morphology

One requirement of the lens material is that the lens allow a high visible light transmission from the outer to inner surface of the lens. A lens morphology which includes large phase separated regions will reduce visible light transmission and cause substantial undesirable image distortion, thereby destroying the value of the lens as a vision correction device. Thus, the lens must have a morphology which allows at least about 80%, more preferably about 90%, visible light transmission and does not produce any significant undesirable image distortion.

In one preferred embodiment, the lens material has at least two phases: the phases including at least one oxyperm phase and at least one ionoperm phase. While there may be two distinct phases, it is believed that there may be a transition phase, or interphase, in which the material composition and the material properties are a blend of those of the oxyperm and ionoperm materials. Thus, there may exist a distinct oxyperm phase or plurality of distinct oxyperm phases, a distinct ionoperm phase or a plurality of distinct ionoperm phases, and an amphipathic phase mixture or blend of oxyperm and ionoperm phases. In one preferred embodiment, the glass transition temperature (Tg) of the oxyperm phase is less than about −115° Celsius.

The existence of separate oxyperm and ionoperm phases, rather than a complete blend of oxyperm and ionoperm phases, is believed to be advantageous in promoting the diffusion of oxygen and ions. Oxygen will diffuse predominantly through the oxyperm polymer, while the ionoperm polymer provides a higher barrier to oxygen diffusion. Similarly, ions will diffuse well through the ionoperm polymer, but the oxyperm polymer provides a higher resistance to ion diffusion. Thus, one homogeneous oxyperm/ionoperm phase will provide undesirable resistance to both oxygen and ion diffusion, while two separate oxyperm and ionoperm phases will provide low resistance pathways for transmission of both oxygen and ions or water. Thus, the ideal extended-wear lens has a pathway or series of pathways from the outer surface to the inner surface for transmission of oxygen therethrough, and an analogous continuous pathway or series of pathways for transmission of water or ions therethrough. In a particularly preferred embodiment, the lens has two co-continuous phases, one an oxyperm phase and the other an ionoperm phase, allowing for permeation of water or ions and oxygen between the front and base curves of the lens.

E. Bulk Water Content

The measurement of water content is difficult because the removal of adhered surface droplets, without affecting the

bulk lens water content, is difficult. In addition, water may evaporate from the lens surface quickly, thereby lowering the water content from the equilibrium level. Accordingly, a discussion of the bulk water content of a lens warrants a discussion of the measurement technique used to determine the water content.

The preferred bulk water content of the hydrated lens will be a function of the lens material properties. The material properties are dependent on the prepolymerization macromers and monomers and polymerization conditions. Thus, the preferred water content for a lens including a fluorine-containing oxyperm material may be different from that of a lens including a siloxane-containing oxyperm material. Accordingly, while general ranges for bulk water content are offered for a better understanding of the invention, the invention is not generally limited to specific bulk water contents.

One method of measuring the water content of a lens formed in accordance with the present invention, referred to herein as the "Bulk Technique" is as follows. First the lens is thoroughly hydrated in a physiological saline solution, such that the water in the lens is in equilibrium with the surrounding water. Next the lens is gently blotted between two lint-free blotting cloths to remove surface moisture. The lens is quickly placed on an aluminum weighing pan and the first wet weight, W_1, is measured. Next, the aluminum pan with lens is placed in a oven at 36° C. for a period of at least 24 hours. After heat treating, the pan with lens is removed, placed in a desiccator, and allowed to cool to room temperature (about 22° C.). The pan with lens is weighed again to determine the dry weight, W_d. The lens is re-equilibrated in physiological saline solution and a second wet weight W_2 is determined thereon. The wet weights (W_1 and W_2) are averaged to yield an average wet weight, W_w. The bulk water content is determined by the following equation:

$$\text{Percent water content}=(W_w-W_d)/W_w \times 100$$

A preferred lens bulk water content, determined by the "Bulk Technique" is less than about 32 weight percent. More preferably, the lens has a water content of about 10 to 30 weight percent, based on the total lens weight. A particularly preferred lens water content is about 15 to about 25 weight percent.

F. Ion and Water Permeability

Unexpectedly, it has been determined that the ion permeability through the lens correlates well with on-eye movement. As discussed earlier, it is known that on-eye movement of the lens is required to ensure good tear exchange, and ultimately, to ensure good corneal health. While the invention is not bound by theory presented herein, it may be useful to discuss some theory for a better understanding of ways to practice the invention.

It is theorized that water permeability is an exceptionally important feature for an extended-wear lens which includes oxyperm polymers such as those disclosed herein. Siloxane-containing oxyperm materials tend to adhere strongly to the eye, thereby stopping on-eye movement. The ability to pass water through the lens is believed to allow a siloxane-containing polymeric lens to move on the eye, where the movement occurs via forces exerted by water being sqeezed out of the lens. The water permeability of the lens is also believed important in replenishing lens water content once pressure is removed. Further, the permeability of ions is believed to be directly proportional to the permeability of water. Thus, ion permeability is a predictor of on-eye movement.

However, regardless of whether the water permeability theory is a correct understanding of the actual on-eye movement phenomenon, it has been unexpectedly found that above a certain threshhold of ion permeability through a lens, from the inner surface of the lens to the outer, or vice versa, the lens will move on the eye, and below the threshhold the lens will adhere to the eye. Thus, the present innovative extended-wear contact lenses provide a balance between the relatively high oxygen permeability (and associated high binding capacity) of oxyperm materials with the low binding capacity (high on-eye movement) of ionoperm materials. It is believed that this is accomplished by providing a plurality of continuous ion transmission pathways for ion and water movement through the lens.

It should be noted that ions may move through the lens via these ion pathways by a number of means. For example, ions may diffuse through the lens because of concentration differences from one surface to another. Ions may also be forced through the ion pathways by the mechanical action of blinking, with the concomittent compression forces on the lens essentially squeezing water out of the lens. In addition, the charge nature of the surfaces may provide an electromotive force which drives ion permeation through the lens. At times, one of these driving forces may be larger than the others, while at other times the relative magnitude may reverse. This discussion is presented to clarify that the invention is not restricted by the method or driving force by which ions move through the lens.

Neither the measurement of water permeability nor ion permeability through an ophthalmic lens is considered a routine matter of testing in the industry. Accordingly, a discussion of the preferred ion or water permeability ranges warrants a discussion of the measurement techniques used to determine the permeability.

The water permeability of a lens may be determined from the rate of water permeation through the lens, from one surface to another surface. The water permeability of a lens may be determined by positioning a lens between two reservoirs holding solutions having known, and different, initial concentrations of radiolabeled water (e.g., tritiated water), and then measuring concentration of radiolabeled water in the "receiving" reservoir (the reservoir towards which the net flow of radiolabeled water is positive) as a function of time.

The relative ion permeability of a lens may be determined from the rate of ion permeation through the lens, from one surface to another surface. The rate of ion permeation may be determined by positioning a lens between two reservoirs holding solutions having known, and different, initial ion concentrations, and then measuring conductivity in the "receiving" reservoir (the reservoir towards which the net flow of ions is positive) as a function of time. The concentration of ions, such as sodium, can be measured accurately using a pH meter and an ion-selective electrode. Ions are believed to be transmitted through a lens, from inner to outer surfaces and vice versa, primarily by the diffusion of ions through water pathways in the lens. Ion permeability through a lens is believed to be directly proportional to water permeability through a lens.

1. Ionoflux Measurement Technique

The following technique, referred to herein as the "Ionoflux Technique", is a preferred method for determining the ion permeability of a lens. This technique may be used to determine the likelihood of adequate on-eye movement.

The "Ionoflux Technique" involves the use of a conductometer (LF 2000/C, catalog no. 35 300105, Wissenschaftlich-Technische Werkstätten GmbH (WTW), Germany), an electrode equipped with a temperature sensor (LR 01/T, catalog no. 302 520, WTW), a donor chamber

containing a salt solution, a receiving chamber containing about 60 ml of deionized water, a stir bar and a thermostat.

The donor chamber is specially designed for sealing a contact lens thereto, so that the donor solution does not pass around the lens (i.e., ions may only pass through the lens). The donor chamber is composed of a glass tube which is threaded at the end which is immersed in the receiving solution. The glass tube includes a centrally located hole of about 9 mm in diameter. A lid, which is threaded to mate with the glass tube, holds a lens-retaining member which includes a centrally located hole of about 8 mm in diameter. The lens-retaining member includes a male portion adapted to mate with and seal the edges of the inner (concave) surface of a lens and a female portion adapted to mate with and seal the edges of the outer (convex) surface of a lens.

The lens to be measured is placed in the lens-retaining member, between the male and female portions. The male and female portions include flexible sealing rings which are positioned between the lens and the respective male or female portion. After positioning the lens in the lens-retaining member, the lens-retaining member is placed in the threaded lid. The lid is screwed onto the glass tube to define the donor chamber. The donor chamber is filled with 16 ml of 0.1 molar NaCl solution. The receiving chamber is filled with 60 ml of deionized water. The leads of the conductivity meter are immersed in the deionized water of the receiving chamber and a stir bar is added to the receiving chamber. The receiving chamber is placed in a thermostat and the temperature is held at about 35° C. Finally, the donor chamber is immersed in the receiving chamber.

Measurements of conductivity are taken every 20 minutes for about three hours, starting 10 minutes after immersion of the donor chamber into the receiving chamber. The Ionoflux Diffusion Coefficient, D, is determined by applying Fick's law as follows:

$$D=-n'/(A\times dc/dx)$$

where

n'=rate of ion transport [mol/min]

A=area of lens exposed [mm^2]

D=Ionoflux Diffusion Coefficient[mm^2/min]

dc=concentration difference [mol/L]

dx=thickness of lens [mm]

An Ionoflux Diffusion Coefficient of greater than about 1.5×10^{-6} mm^2/min is preferred for achieving sufficient on-eye movement. More preferably, the Ionoflux Diffusion Coefficient is greater than about 2.6×10^{-6} mm^2/min, while most preferably, the Ionoflux Diffusion Coefficient is greater than about 6.4×10^{-6} mm^2/min. It must be emphasized that the Ionoflux Diffusion Coefficient correlates with ion permeability through the lens, and thereby is a predictor of on-eye movement.

2. Ionoton Measurement Technique

The following technique, referred to herein as the "Ionoton Technique", is another preferred method for determining the relative ion permeability of a lens. The technique is based on measurement of the diffusion of sodium chloride through a lens.

The "Ionoton Technique" involves the use of a pH meter (Beckman, VWR catalog no. BK123142), a VSC-1 Diffusion Cell Drive Console (Crown-Bio, Somerville, N.J.), a DCB-100B Diffusion Cell (Crown-Bio), and a 6 cm sodium ion-specific electrode (Microelectronics, Londonderry, N.H., catalog no. MI-414P). The technique is not limited to the aforementioned instruments or materials; equivalent instruments or materials may be used.

First, a contact lens is mounted onto an orifice of the DCB-100B cell chamber, the donor chamber. Next, the connecting cell chamber (receptor chamber) is placed against the cell chamber containing the contact lens and tightly clamped on the clamp holder supplied with the VSC-1 Drive Console. Then, a phosphate-buffered saline (PBS, Mediatech catalog no. 21-031-LV) is placed into the receptor side of the cell chamber. Stir bars are added to each cell chamber. The 6 cm electrode is placed into the PBS saline receptor side. After the electrode has equilibrated in the PBS saline, the pH meter is placed in the mV function to establish the 0 mV point. PBS which has been saturated with sodium chloride is added to the donor chamber.

The millivolt signal is recorded at 5, 10, 15, 30, 60, 120, and 180 minute intervals. The millivolt signal is converted to a sodium ion concentration by a standard curve of sodium ion concentration vs. millivolt signal. The Ionoton Ion Permeability Coefficient, P, is then determined in accordance with the following equation:

$$\ln(1-2C(t)/C(0))=2APt/Vd$$

where:

C(t) concentration of sodium ions at time t in the receiving cell

C(0)=initial concentration of sodium ions in donor cell

A=membrane area, i.e., lens area exposed to cells

V=volume of cell compartment (3.0 ml)

d=average lens thickness in the area exposed

P=permeability coefficient

The average thickness of the lens in the exposed test area may be determined by averaging a number of readings, e.g., 10 readings, with a low-pressure thickness-measuring instrument, such as a Mitotoya micrometer VL-50, or equivalents thereof. The Ionoton Ion Permeability Coefficient, P, having units of cm^2/second, may be determined from the slope of a plot of time (t) v.$\ln(1-2C(t)/C(0))\times(-2At/Vd)$.

An Ionoton Ion Permeability Coefficient, P, of greater than about 0.2×10^{-6} cm^2/sec is preferred, while greater than about 0.3×10^{-6} cm^2/sec is more preferred and greater than about 0.4×10^{-6} cm^2/sec is most preferred. It must be emphasized that the Ionoton Ion Permeability Coefficient correlates with ion permeability through the lens, and thereby is a predictor of on-eye movement.

3. Hydrodell Water Permeability Technique

The following technique, referred to herein as the "Hydrodell Technique" is a preferred method for determining the water permeability of a lens. This technique may be used to determine the likelihood of adequate on-eye movement.

The Hydrodell Technique involves the measurement of the rate of transfer of the radiolabeled solutes THO (^{3}H—HO or tritiated water) and ^{14}C-glucose across the contact lens using a two-chamber apparatus. ^{14}C-glucose is used in this measurement technique to reveal any leak in the system during testing. The lens is mounted between chambers, which are stirred at a controllable rate. Chamber I contains a solution with a high concentration of labeled solute. Chamber II, the "receiving chamber" contains an identical solution but without the labeled solute. Samples of the solution in chambers I and II are taken at intervals over the test period. The radioactivity in the samples is measured. The permeability of the lens is calculated from the measured radioactivity, the sample times, the chamber volumes and the lens area exposed to the solutions. A more detailed description of the Hydrodell Technique follows.

a. Solution Preparation

Dulbecco's phosphate buffered saline (DPBS) is prepared by first dissolving, sequentially, about 160 g sodium chloride (NaCl), about 4 grams potassium chloride (KCl), about 23 grams disodium hydrogen orthophosphate (Na_2HPO_4), about 4 grams potassium dihydrogen orthophosphate (KH_2PO_4), and about 10 grams sodium azide in a liter of reverse-osmosis (MilliQ) water. Then, the pH is adjusted to about 7.3 by adding appropriate amounts of HCl. Finally, the buffer solution is diluted to 1:20 (50 ml buffer solution with 950 ml reverse-osmosis water). and allowed to degas either in a screw-capped container overnight or under vacuum.

A Cold Glucose buffer solution is prepared by adding about 0.1 grams D-glucose to one liter of DPBS, followed by sterilization via filtration through a 0.2 μl millipore filter and storage at 4° C. until use.

The Chamber I solution is prepared by adding about 6 μl THO (TR53, 1.0 mCi/ml activity, available from Amersham Australia, located in North Ryde NSW Australia) and about 16 μl ^{14}C-glucose THO (in ethanol, available from Amersham Australia) to about 12 ml of the Cold Glucose buffer solution. Preferably, this solution is used within about 24 hours of preparation. The Chamber II solution is DPBS.

b. Apparatus Preparation

The chambers have a volume sufficient to hold about 12 ml of solution during testing. While the exact shape of the chambers is not critical, both chambers have rectangular cross-sections for ease of construction. The chambers may be made from a variety of water-proof rigid materials, preferably clear (e.g., acrylic plates, FX Plastics, Marrickville NSW Australia) so that samples may be observed during testing. Each chamber has a circular aperture of about 7 mm diameter appropriate for mounting a lens between the chambers for contact with solutions held withing the chambers. Some affixing means, such as a set of mounting bolts, are necessary to securely affix one chamber to the other with the lens mounted in between.

A test contact lens is mounted symmetrically over the aperture of Chamber II. Folds and wrinkles are manually removed from the lens. Chamber I is positioned adjacent the aperature and mounted lens of Chamber II, and the chambers are secured to one another using mounting bolts.

About 12 ml (V_2) of DPBS is placed in Chamber II. About 12 ml of the Chamber I labeled solution is placed in Chamber I, at which point time t=0 is established. Stirrers are added to both chambers and the stirrer speed is set at about 1200 rpm.

c. Sampling

Sampling generally starts at time t_0=5 minutes. The final sample time, t_f, is usually at about 50 minutes for high water content lenses and about 120 minutes for low water content lenses, although these times are not critical.

At time t_0=5 minutes, two samples of about 0.2 ml volume are pipetted from Chamber I, and two 0.2 ml aliquots of DPBS are added to Chamber I to restore the volume. These samples are placed into plastic counting tubes with about 4 ml Ultima Gold™ cocktail (available from Packard Instrument Co., Meriden, Conn.) and about 0.9 ml DPBS.

Also at time t_0, one sample of about 1.0 ml volume is pipetted from Chamber II and one 1.0 ml aliquot of DPBS is added to Chamber II to restore the volume. The sample is placed into a plastic counting tube with about 4 ml Ultima GoId™ cocktail.

At intermediate times between t_0 and t_f (e.g., every 10 minutes), one sample of about 1.0 ml volume is pipetted from Chamber II and one 1.0 ml aliquot of DPBS is added to Chamber II to restore the volume. Each sample is placed into a plastic counting tube with about 4 ml Ultima Gold™ cocktail.

At time t_f, two samples of about 0.2 ml volume are pipetted from Chamber I. These samples are placed into plastic counting tubes with about 4 ml Ultima Gold™ cocktail and about 0.9 ml DPBS.

Also at time t_f, two samples of about 1.0 ml volume are pipetted from Chamber II. These samples are placed into plastic counting tubes with about 4 ml Ultima Gold™ cocktail.

d. Measurements

The activity of the samples are measured by liquid scintillation counting, or other appropriate technique. Liquid scintillation counting may be advantageously accomplished by using protocol number 6 for ^{3}H/^{14}C on a Tri-Carb Liquid Scintillation Analyzer (1900TR, available from Packard Instrument Co.).

Three standards containing about 10^4 to 10^5 cpm THO in reversed-osmosis (MilliQ) water are prepared. Three standards containing about 10^4 to 10^5 cpm ^{14}C glucose in reversed-osmosis (MilliQ) water are also prepared. A blank containing MilliQ water is prepared.

The scintillation analyzer settings are LLA=0 KeV and ULA=12 KeV for ^{3}H ("1") in channel **1** and LLB=12 KeV and ULB=156 KeV for ^{14}C ("2") in channel **2**. The standards and blank are counted three times during each counting of samples, and the counts are averaged. The following denote the relevant measured sample activities:

b_1=measured activity of blank sample in channel **1**

b_2=measured activity of blank sample in channel **2**

S'_{11}=measured activity of standard ^{3}H sample in channel **1**

S'_{12}=measured activity of standard ^{14}C sample in channel **2**

S'_{21}=measured activity of standard ^{3}H sample in channel **1**

S'_{22}=measured activity of standard ^{14}C sample in channel **2**

y_1=measured activity of test sample (both ^{3}H and ^{14}C) in channel **1**

Y_2=measured activity of test sample (both ^{3}H and ^{14}C) in channel **2**

e. Water Permeability Calculation

In order to calculate the actual activity of a sample, the measured activities of the isotopes, ^{3}H and ^{14}C, must first be corrected to remove the cross-contamination error due to the presence of both isotopes in one sample. Without explaining the mathematical derivations, the following stepwise procedure is offered as an example of one method of determining water permeability from the above measurements:

(1) Calculate S_{11}, S_{12}, S_{21}, and S_{22}, from the following equations:

$$S_{11}=S'_{11}-b_1$$

$$S_{12}=S'_{12}-b_1$$

$$S_{21}=S'_{21}-b_2$$

$$S_{22}=S'_{22}-b_2$$

(2) Calculate a_{12} and a_{21} from the following equations:

$$a_{12}=S_{12}/S_{22}$$

$$a_{21}=S_{21}/S_{11}$$